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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/522,753	03/10/2000	Ronald M. Evans	SALK1510-3	4924

30542 7590 03/06/2007

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/522,753	EVANS ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,14,16,18-23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3,4 and 19-22* is/are allowed.

6)☒ Claim(s) *5,14,16,23 and 25* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 12/20/2006, in which claims 1-2, 6-13, 15, 17, 24 and 26-38 were canceled, and claims 3-5, 14, 23 and 25 were amended. Currently, claims 3-5, 14, 16, 18-23 and 25 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group I (claims 3-5, 14, 16 and 18-25, as they read on SEQ ID NOS: 4 and 5) with traverse in the reply filed on 1/17/2006. Currently, claims 3-5, 14, 16, 18-23 and 25 are under consideration as they read on SEQ ID NOS: 4 and 5.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The prior application to which the instant application seeks

priority is U.S. Application Serial No. 08/522,726, filed 9/1/1995 (now U.S. Patent No. 6,489,441). The '726 application discloses only 3 sequences that correspond to SEQ ID NOS: 1-3 of the instant application. Each of the pending claims is directed to an isolated polynucleotide that (i) has a recited percent identity to one of SEQ ID NOS: 4, 6, & 8; or (ii) encodes a polypeptide having a recited percent identity to one of SEQ ID NOS: 5, 7 & 9. The prior application does not disclose these particular sequences. Therefore, the prior application does not provide support for the broadly recited genus of polynucleotides encompassed by the pending claims. Accordingly, the priority date for the pending claims is the filing date of the instant application (3/10/2000).

Applicant's arguments filed 9/20/2005 have been fully considered but they are not persuasive. The response asserts that the prior application discloses co-suppressors of steroid/thyroid hormone receptor activity having defined amino acid residues, or conservative variations thereof, and that the present application properly claims priority because the human SMRT sequence disclosed in the present application is an extension of the sequence information disclosed in the parent application. The response notes that the present application includes "newly discovered SMRT sequence information." Further, the response asserts that the sequence information disclosed in the parent application, and disclosed and claimed in the present application that is entitled to the priority date of the parent application. This is not found persuasive because the instant claims encompass sequences not disclosed in the parent application. Thus, the sequences of the parent application do not provide support under 35 USC 112, first paragraph, for the full scope of any of the present claims. As discussed above, the

parent application does not disclose SEQ ID NOS: 4 and 5. Thus, the effective filing date of the present claims is 3/10/2000.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 23 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al (Nature, October 1995, Vol. 377, No. 6548, pages 454-457, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/23/2005 and has been rewritten to address the amendment of the claims in the reply filed 12/20/2006. The rejection has been extended to claims 23 and 25, which was necessitated by the amendment of the claims.

Chen et al teach the identification and characterization of a transcriptional co-repressor that is a SMRT (i.e. silencing mediator for retinoid and thyroid hormone receptors). The SMRT polypeptide taught by Chen et al is encoded by a polynucleotide sequence that encodes a polypeptide that is ~94% identical to the sequence of SEQ ID NO: 5 (see Exhibit A, result #6 for accession number HSU37146, mailed 5/23/2005). The nucleotide sequence of HSU37146, encodes a protein that has less than 83% identity with a Sin3A interaction domain of N-CoR as set forth as amino acids 255 to 312 of SEQ ID NO: 11, has less than about 57% identity with the repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11, has less than

about 66% identify with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11, and has less than bout 30% identity with repression domain 2 of N-CoR set forth as amino acids 736-1031 of SEQ ID NO: 11 (see Exhibits I-VI, where the amino acid sequence of HSU37146 (AAC50236.1) is compared to the claimed regions of human N-CoR as set forth in O75376, which is 100% identical to instant SEQ ID NO: 11). Further, Chen et al teach a plasmid comprising a nucleic acid sequence encoding a SMRT-GAL4 DNA binding domain fusion protein (e.g. paragraph bridging pages 456-457; Figure 4). Thus, the polynucleotide sequence taught by Chen et al anticipates the broad genus of polynucleotides encompassed by the instant claims. The nucleic acid sequence of HSU37146 is a sequence that has at least 80% sequence identity with SEQ ID NO: 4, encodes at least five contiguous amino acids of amino acids 720-745 of SEQ ID NO: 5, and does not hybridize to a polynucleotide encoding SEQ ID NOS: 9 or 11 under high stringency conditions.

Claims 5, 23 and 25 are rejected under 35 U.S.C. 102(a) as being anticipated by Park et al (PNAS USA, 30 March 1999, Vol. 96, No. 7, pages 3519-3524, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/23/2005 and has been rewritten to address the amendment of the claims in the reply filed 12/20/2006. The rejection has been extended to claims 23 and 25, which was necessitated by the amendment of the claims.

Park et al teach the identification of an extended isoform of SMRT termed SMRTe by the authors. In particular, Park et al teach nucleic acids, described by accession numbers AF125672 & AF125671, that encode polypeptides with ~98% and ~82% identity with SEQ ID NO: 5 (e.g. see results 2 & 4 of the search report provided as Exhibit A, mailed 5/23/2005). The nucleic acid

sequence of AF125672 encodes a protein with 63% identity to amino acids 1-312 of SEQ ID NO: 11 (see Exhibit I). The nucleic acid sequence of AF125671 encodes a protein with 56% identity to amino acids 1-312 of SEQ ID NO: 11 and 60% identity to amino acids 312-668 of SEQ ID NO: 11 (see Exhibits VII & VIII, respectively). Further, the nucleic acid sequence of AF125672 is 97% identical to the nucleic acid sequence of SEQ ID NO: 4 (see Exhibit IX). Moreover, the nucleic acid sequence of AF125672 is 98% identical to nucleotides 1-3094 of SEQ ID NO: 4 (see Exhibit X). Park et al teach a polynucleotide comprising a sequence encoding the N-terminal sequence of SMRTe (aa 1-1111) operatively linked to a Gal4 DNA binding domain in a plasmid expression construct, which was transfected into HeLa cells to determine assay repression activity (e.g. page 3522, left column, 2nd paragraph; page 3520, left column, 1st full paragraph; page 3524, left column, 1st paragraph; Figure 3). Further, Park et al teach the SMRTe nucleic acid sequence in the pBluescript vector (e.g. paragraph bridging pages 3519-3520). The nucleic acid sequence of AF125672 is a sequence that has at least 80% sequence identity with SEQ ID NO: 4, encodes at least five contiguous amino acids of amino acids 720-745 of SEQ ID NO: 5, and does not hybridize to a polynucleotide encoding SEQ ID NOS: 9 or 11 under high stringency conditions.

Response to Arguments - 35 USC § 102

The rejection of claims 3, 4 and 19-22 under 35 U.S.C. 102(b) as being anticipated by Chen et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/20/2006.

With respect to the rejection of claims 5, 23 and 25 under 35 U.S.C. 102(b) as being anticipated by Chen et al, Applicant's arguments filed 12/20/2006 have been fully considered but they are not persuasive.

The response asserts that the prior art sequences must be compared to the claimed sequence using a global alignment procedure rather than a local alignment procedure. This is not found persuasive, because the specification does not specifically define "sequence identity" to mean global percent identity, and the claims do not require a global alignment. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., global alignment or percent identity over a particular range of nucleotides of SEQ ID NO: 4) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 4 requires an isolated polynucleotide to encode a protein with the claimed function and at least 80% identity with SEQ ID NO: 4. The sequence of Chen et al encodes a protein of the claimed function and is 80% identical to SEQ ID NO: 4. Given the broadest reasonable interpretation the term "80% sequence identity with SEQ ID NO: 4" encompasses polynucleotides with 80% identity to SEQ ID NO: 4 as demonstrated with a local alignment procedure.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

The rejection of claims 3, 4, 14 and 19-22 under 35 U.S.C. 102(a) as being anticipated by Park et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/20/2006.

With respect to the rejection of claims 5, 23 and 25 under 35 U.S.C. 102(a) as being anticipated by Park et al, Applicant's arguments filed 12/20/2006 have been fully considered but they are not persuasive.

The response asserts that Park et al merely published findings similar to those reported by Applicants in Ordentlich et al (PNAS, Vol. 96, No. 6, pages 2639-2644) two weeks after the publication of the Ordentlich reference. The response asserts that the earlier publication of Ordentlich demonstrates that Applicants were in possession of the present invention before the effective date of the Park publication. This is not found persuasive because the sequences disclosed in the Ordentlich and Park references are not identical. The sequences disclosed by Ordentlich et al are not sufficient to describe the broadly claimed genus. The sequences disclosed by Park et al are not obvious variants of the sequences disclosed by Ordentlich et al. Thus, the Ordentlich reference does not provide evidence that Applicant's were in possession of the invention disclosed by Park et al prior to the date of the Park reference.

Based upon the claim amendments, the response requests the withdrawal of the rejection over claims 4, 19 and 21-22 (page 9, paragraph 1). As noted above, the rejection has been withdrawn for claims 4, 19 and 21-22. The rejection is maintained for claim 5 and has been extended to claims 23 and 25.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

The rejection of claims 23 and 25 under 35 U.S.C. 102(a) as being anticipated by GenBank Accession Number NM_002900.1 (GI: 4506452, 3/19/1999) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/20/2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was made in the Office action mailed 9/22/2006 and has been rewritten to address the amendments to the claims in the reply filed 12/20/2006.

The claims are drawn to a genus of oligonucleotide comprising at least 15 nucleotides that must meet specific functional limitations of the claims. The claims require the oligonucleotides to be capable of performing the following functions: (i) hybridizing "under high stringency conditions" to the polynucleotide of claim 4, which is a polynucleotide that encodes a SMRT co-repressor, wherein said SMRT co-repressor or portion thereof is capable of mediating transcriptional silencing and has the sequence of SEQ ID NO: 5 or conservative variations thereof, and (ii) does not hybridize to a polynucleotide encoding SEQ ID NO: 11. Thus, the genus of oligonucleotides must be capable of hybridizing to a genus of polynucleotides defined

SEQ DI NO: 5 and conservative variants thereof, while not being able hybridize to a genus of polynucleotides defined by the ability to encode the protein of SEQ ID NO: 11. The polynucleotides that encode the amino acid sequence of SEQ ID NO: 11 are many due to the degeneracy of the genetic code. Claim 25 further requires the oligonucleotide to hybridize to a genus of polynucleotides encoding SEQ ID NO: 5 without hybridizing to a genus of polynucleotides encoding SEQ ID NO: 9. Further, the oligonucleotide must encode at least five consecutive amino acids of a sequence selected from amino acids 720 to 745 of SEQ ID NO: 5. Thus, he rejected claims thus comprise a set of oligonucleotides that encompass specific functional limitations with regard to the ability to hybridize to one genus of sequences without hybridizing to another genus of sequences.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. At page 17, lines 16-28, the specification envisions the following with regard to oligonucleotides:

> Additional examples of invention isolated oligonucleotides, are those which generally are at least about 15 nucleotides in length and can hybridize specifically to the polynucleotide of the invention, but not to a polynucleotide encoding an N-CoR polypeptide (SEQ ID NO: 11). An oligonucleotide of the invention can be useful as a probe, or as a primer for a PCR procedure, or can encode a peptide containing at least five contiguous amino acids of a SMRT co-repressor. In one embodiment, an oligonucleotide of the invention encodes at least five contiguous amino acids of a sequence such as that shown as amino acids 720 to 745 of SEQ ID NO: 5, or amino acids 716 to 742 of SEQ ID NO: 7; or amino acids 497 to 523 of SEQ ID NO: 9. In another embodiment, an oligonucleotide of the invention can hybridize specifically to a polynucleotide encoding human SMRT (SEQ ID NO: 5) or mouse SMRTα

(SEQ ID NO: 7), and, optionally, to a polynucleotide encoding mouse SMRTβ (SEQ ID NO: 9).

No description is provided of any oligonucleotide that meets the functional limitations of the claims other than the disclosed nucleic acid sequence of SEQ ID NO: 4, which would hybridize to itself (i.e., it encodes at least five consecutive amino acids of SEQ ID NO: 5), and presumably would not hybridize to a nucleic acid encoding SEQ ID NO: 11 or SEQ ID NO: 9 given the potential to mutate each codon to produce a variant sequence that would not hybridize under "high stringency". Given the related nature of the N-CoR protein of SEQ ID NO: 11 and the SMRT co-repressor of SEQ ID NO: 5, one cannot envision a representative number of oligonucleotides that would be capable of hybridizing to polynucleotides of claim 4 without hybridizing to the polynucleotides encoding SEQ ID NO: 11 or SEQ ID NO: 9.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of oligonucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of oligonucleotides encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the specific nucleotide sequences that one could use to design oligonucleotides that meet the functional limitations of the claims, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of oligonucleotides. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those oligonucleotides that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 23 and 25.

Claims 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a SMRT co-repressor, where the polynucleotide comprises a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 3094 of SEQ ID NO: 4, does not reasonably provide enablement for these nucleotide sequences, which also must not encode "a sequence" (i.e., two or more amino acids)

of SEQ ID NO: 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection was made in the Office action mailed 9/22/2006 and has been rewritten to address the amendments to the claims in the reply filed 12/20/2006.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to polynucleotides that encode a SMRT co-repressor, wherein the SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Claim 14 is drawn to a polynucleotide comprising a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 3094 of SEQ ID NO: 4, provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11. The polynucleotide cannot contain "a sequence" identical to SEQ ID NO: 11. Thus, the claimed sequence cannot encode a protein with 2 or more contiguous amino acids in common with SEQ ID NO: 11. Claim 16 is drawn to a polynucleotide comprising nucleotides 1 to 3094 of SEQ ID NO: 4, and a polynucleotide having 80% sequence identity with the complementary sequence of nucleotides 1 to 3094 of SEQ ID NO: 4. The nature of the invention is complex in that all of the claimed polynucleotides must not encode a protein with "a sequence" found in SEQ ID NO: 11.

Breadth of the claims: The claims are broad in that they are drawn to coding sequences and complements thereof defined by percent identity.

Guidance of the specification and existence of working examples: The specification teaches that the polynucleotide of SEQ ID NO: 4 encodes a human SMRT co-repressor (SEQ ID NO: 5; e.g. page 9, lines 15-22). The specification teaches that the N-terminal region of the protein encoded by SEQ ID NO: 4 can modulate the transcriptional potential of a nuclear receptor, particularly a nuclear receptor that is in the form of a dimer, for example, a thyroid hormone receptor homodimer, a retinoic acid receptor homodimer, a retinoid X receptor homodimer, etc. (e.g. paragraph bridging pages 9-10). Specifically, amino acids 1-1031, 1-303 and 736-1031, and the SANT domain of SEQ ID NO: 5 confer a significant amount of repression (e.g. Example 11). Based upon the teachings of the specification, it is within the skill of the art to use the nucleotide sequence of SEQ ID NO: 4, or a nucleotide sequence having at least 80% sequence identity to SEQ ID NO: 4 to encode a protein with nuclear hormone repression activity (e.g. Figure 9).

Predictability and state of the art: It would be unpredictable to make and use the claimed invention because the claimed sequence cannot encode a protein with two or more contiguous amino acids in common with SEQ ID NO: 11.

Amount of experimentation necessary: The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to teach how to make and use any nucleic acid that encode a polypeptide having SMRT co-repressor activity and also lacks a sequence of SEQ ID NO: 11. The likelihood of one being able to make a nucleic acid that meets each of the limitations of the claims is

exceedingly low.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 14 and 16 are not considered to be fully enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was made in the Office action mailed 5/23/2005 and has been rewritten to address the amendments to the claims filed 12/20/2006.

Claim 23 is vague and indefinite in that the metes and bounds of the phrase "high stringency conditions" are unclear. The phrase is used in the context of an identified oligonucleotide comprising at least 15 nucleotides encoding at least 5 amino acids of amino acids 720-745 of SEQ ID NO: 5 and that hybridizes to a polynucleotide of claim 4, but not to a polynucleotide encoding SEQ ID NO: 11. The use of "high stringency conditions" renders the claim(s) vague and indefinite, because there is no clear art-recognized definition for the term, and the specification fails to set forth a clear definition. Thus the metes and bounds of the conditions encompassed by the term are unclear.

Claim 25 recites "high stringency conditions" and depends from claim 23. Thus, claim 25 is indefinite for the same reasons applied to claim 23.

Response to Arguments - 35 USC § 112

The rejection of claims 23-25 under 35 U.S.C. 112, first paragraph (new matter) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/20/2006.

With respect to the rejection of claims 23 and 25 under 35 U.S.C. 112, first paragraph (written description), Applicant's arguments filed 12/20/2006 have been fully considered but they are not persuasive.

The response essentially asserts that the scope of claim 4 has been narrowed such that it would be a simple matter for one to perform a multiple sequence alignment to identify those oligonucleotides that meet the requirements of the claims. While the genus of sequences encoding the SMRT polypeptide of SEQ ID NO: 5 has been narrowed by the amendment, the genus of sequences that encode the polypeptides of SEQ ID NOS: 11 and 9 remain enormous. For example, SEQ ID NO: 11 is 2,440 amino acids in length. The only amino acid for which there is a single codon is methionine. The other amino acids are encoded by multiple different codons (e.g., leucine, serine and arginine are encoded by six different codons, and proline, threonine, alanine and glycine are encoded by four different codons; see the attached amino acid table printed from http://algoart.com/aatable.htm on 2/28/2007). Thus, over thousands of codons, the potential nucleic acid sequences encompass an enormous genus, each of which must be compared to the genus of sequences encoding SEQ ID NO: 5 and conservative variants thereof. Accordingly, the specification does not provide adequate written description of the invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of oligonucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claims 14 and 16 under 35 U.S.C. 112, first paragraph (enablement), Applicant's arguments filed 12/20/2006 have been fully considered but they are not persuasive.

The response essentially asserts that the amendments to the claims have overcome the rejection. The amendment to the claims has overcome the rejection with respect to the complementary sequences. However, the amended claims require the nucleic acid sequence encoding the SMRT co-repressor to lack any sequence in common with SEQ ID NO: 11. Thus, the amendments to claims are insufficient to overcome the rejection.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

The rejection of claims 3, 14, 16, 24 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/20/2006.

With respect to the rejection of claims 23-25 under 35 U.S.C. 112, second paragraph, Applicant's arguments filed 12/20/2006 have been fully considered but they are not persuasive. The response asserts that one of skill in the art could readily identify "suitable" conditions to accomplish the desired goal. This is not found persuasive, because there is no clear art-recognized definition for the term "high stringency," and the specification fails to set forth a clear definition. Thus the metes and bounds of the conditions encompassed by the term are unclear.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

Claims 3, 4 and 19-22 are allowed.

Claim 18 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CELINE QIAN, PH.D.
PRIMARY EXAMINER

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad